

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
14 March 2002 (14.03.2002)

PCT

(10) International Publication Number
WO 02/20089 A1

(51) International Patent Classification⁷: **A61N 5/10**,
A61M 36/12

(74) Agents: **VAN KAN, J., J., H.** et al.; Algemeen Oc-
trooibureau, World Trade Center, Pastoor Petersstraat 160,
NL-5612 LV Eindhoven (NL).

(21) International Application Number: **PCT/NL01/00647**

(22) International Filing Date:
3 September 2001 (03.09.2001)

(25) Filing Language: **Dutch**

(26) Publication Language: **English**

(30) Priority Data:
1016101 5 September 2000 (05.09.2000) **NL**

(71) Applicant (for all designated States except US): **NUCLE-
TRON B.V.** [NL/NL]; Waardgelders 1, NL-3905 TH Vee-
nendaal (NL).

(72) Inventors: and

(75) Inventors/Applicants (for US only): **VISSCHER, Arie,**
Luite [NL/NL]; Verheulalaan 13, NL-3971 RD Driebergen
(NL). **LÖFFLER, Edgar, German** [DE/DE]; Amalien-
park 4, 13187 Berlin (DE).

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE,
DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,
PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

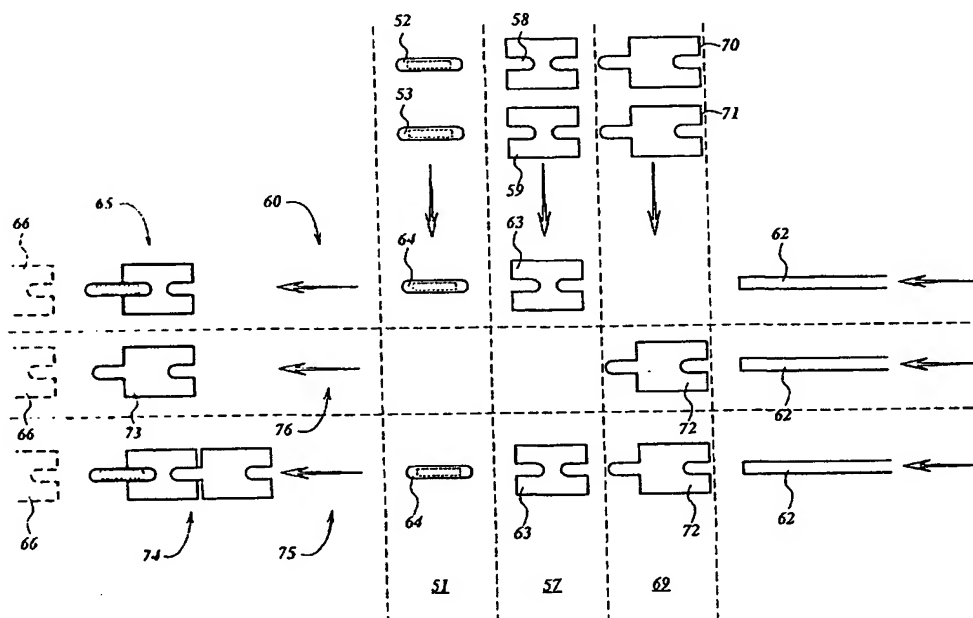
(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG).

Published:

— with international search report

[Continued on next page]

(54) Title: **ROW OF RADIOACTIVE SEEDS AND NON-RADIOACTIVE SPACERS AND CONNECTORS THEREFORE**



(57) Abstract: An arranged row of radioactive seeds and non-radioactive spacers with a predetermined pitch can be provided with physical coherence by applying connectors between the separate seeds and spacers. In a first embodiment the connectors are elongated with introversions at both ends, in a second embodiment a connector also forms a spacer and is provided at one end with an introversion and at another end with a projection in the form of a seed.

WO 02/20089 A1



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Row of radioactive seeds and non-radioactive spacers and connectors therefore.

The invention relates to a row of radioactive seeds and non-radioactive spacers arranged with a predetermined pitch, in which the number of spacers can be zero, for a brachytherapeutic treatment of an animal body with radioactive radiation, which seeds have elongated shapes.

Such a row is known from Dutch patent application 1012697 and American patent application S/N 09/377,382.

Therein is disclosed a device for composing a row of radioactive seeds and non-radioactive spacers, in which the number of spacers can be zero, for a brachytherapeutic treatment of tissue with radioactive radiation. The seeds disclosed therein have an elongated shape. By means of the device disclosed in the above mentioned patent applications the row of radioactive seeds and non-radioactive spacers is entered into a hollow needle with an open end which open end has been temporarily closed with a plug of wax. After the row of radioactive seeds and non-radioactive spacers has been entered into the hollow needle the relevant needle is subsequently inserted in the body comprising the tissue to be irradiated. After the needle with the row of radioactive seeds and non-radioactive spacers has been entered into or near to the tissue to be irradiated a plunger causes the row of radioactive seeds and non-radioactive spacers to remain at its place and the hollow needle is retracted. By retracting the plug of wax is pushed against the row of radioactive seeds and non-radioactive spacers and subsequently the plug releases from the open end of the hollow needle. On further retraction of the hollow needle the complete row of radioactive seeds and non-radioactive spacers is placed in or near to the tissue to be irradiated. Finally, the hollow needle and

the plunger are removed from the body. In this way it is achieved that the row of radioactive seeds and non-radioactive spacers with a predetermined pitch has been placed in the body.

The disclosed manner of inserting a row of radioactive seeds and non-radioactive spacers has a disadvantage in that after the row has been inserted into the body or near to the tissue to be irradiated there is no physical relation anymore between the inserted seeds and spacers other than through the tissue of the body. That may have as a consequence that upon movements of the body in which the row of radioactive seeds and non-radioactive spacers has been inserted the radioactive seeds and non-radioactive spacers may move through the body/the tissue to be irradiated and as a consequence of such movement irradiate other tissue. That may be disadvantageous for the therapeutic treatment since the distribution of radioactive seeds and non-radioactive spacers has been calculated with great accuracy in order to reach an optimal result in respect of the irradiation of the tissue to be irradiated. This is the more important because in general not one but a number or even a great number of rows of radioactive seeds and non-radioactive spacers each arranged with a predetermined pitch, is inserted in order to irradiate the tissue, often cancerous tissue and spare the urethra.

In the context of the present invention, the term "spacer" is defined as an element which substantially has the same form and substantially the same dimensions as the seed, but, contrary to a seed, is not radioactive.

There is a need for rows of radioactive seeds and non-radioactive spacers, arranged with a predetermined pitch, in which the number of spacers can be zero, for brachytherapeutic treatment of tissue with radioactive radiation in which better care can be taken that the mutual spatial arrangements of radioactive seeds and non-

radioactive spacers upon movement of the body cannot mutually change places after insertion of the row into the body.

This object is achieved according to the invention in that connectors are present between successive seeds, which connectors have substantially elongated shapes with two ends, in that at least one end of each connector is provided with an introversion in a longitudinal direction of the connector, in that the introversion has a shape complementary to the shape of a seed and in the longitudinal direction of the connector has a dimension which at most is equal to half the length of a seed.

Thereby it is achieved that the physical coherence is present between successive seeds of a row of radioactive seeds and non-radioactive spacers. The seeds have been coupled to each other "mechanically" in the form of a flexible "chain". Contrary to a normal chain the seeds and the connectors are not fixed together which on the one hand ensures a certain degree of flexibility and on the other hand is not necessary since the tissue to be irradiated and the body, respectively exercise sufficient pressure to cause the seeds to remain pressed into the introversions.

As such US patent 4,815,449 discloses a row of radioactive seeds and non-radioactive spacers arranged with a predetermined pitch, in which the number of spacers can be zero, for a brachytherapeutic treatment of tissue with radioactive radiation, which seeds have elongated shapes. The relevant seeds and spacers are surrounded by elongated cylindrical elements one cross-end of which is provided with a projection and an other cross-end of which is provided with an introversion. The projections have shapes complementary to those of the introversions. Identical elements thus achieved can be connected together into a row of elements. The row of elements come into being in that way has a large degree of stiffness, that is, is not flexible,

and is provided with a sharp tip at the end that is being driven into the body. In this way the elements connected together form a needle with a sharp tip. After insertion of the row of radioactive seeds and non-radioactive spacers, which are present in the elements of the needle thus formed, the relevant needle with the sharp tip remains in the body. A disadvantage thereof is that movements of the body and/or the tissue in which the row of radioactive seeds and non-radioactive spacers, engineered as a needle, has been inserted upon movements on the one hand can be hindered because the needle thus formed is not flexible, that is behaves as a stiff elongated element in the body and on the other side that one of the ends of that stiff element is provided with a sharp tip. Upon movements that sharp tip can easily cause damage to the tissue about the tip causing traumatic tissue reaction. A further disadvantage is that the material from which the cover of the seeds and spacers has been manufactured must be of sufficient stiffness to be able to form a stiff needle. That limits the choice of materials suited for this purpose.

International Patent Application WO 99/59675 discloses a "spacer" element for treating prostate cancer, using an implant of radioactive seeds. The "spacer" element according to WO 99/59675 has a generally cylindrical exterior form and comprises a central section and two cup-like end sections. It is configured in such a way that it fits within a conventional needle, which is loaded with an alternating succession of radioactive seeds and "spacer" elements (with the meaning of WO 99/59675), for subsequent positioning in the prostate. It should be noted that with the "spacer" element according to International Patent Application WO 99/59675 a different element, i.e. a connecting element between two seeds, is meant which differs from the above defined term "spacer" according to the present invention.

International Patent Application WO 00/09211 discloses radioactive seeds provided with "gripping" ends. Such an end fits in a cavity in a bio-absorbable "spacer" according to WO 00/09211. Subsequent seeds are linked together by means of "spacers" according to WO 00/09211 before being loaded in an injection needle, so as to remain connected to each other. It should be noted that with the "spacer" element according to International Patent Application WO 00/09211 a different element is meant which differs from the above defined term "spacer" according to the present invention. The "spacers" according to WO 00/09211 can have different lengths.

The preferred embodiment of a row according to the invention is characterised in that seeds and spacers have identical form and measurements and in that each end of each connector is provided with an introversion in longitudinal direction of the connector and in that each introversion is shaped complementary to the shape of a seed and in a longitudinal direction of the connector has dimensions smaller than half the length of a seed.

Thereby it is achieved that the row can be composed alternately comprising a seed or spacer and a connector. The calculated and desired radiation pattern is achieved by distributing seeds and spacers along the row in the rate calculated and coupling the seeds and spacers by means of the connectors.

A further preferred embodiment of a row according to the invention is characterised in that one or more spacers comprise connectors one end of which is provided with an introversion and an other end of which is provided with a projection having a shape identical to the shape as from an end of a seed.

Thereby it is achieved that on composing an arranged row of radioactive seeds and non-radioactive spacers only one action will be necessary to add one non-radioactive spacer to an already existing row

in which the last element of the row is provided with an introversion and that subsequently through adding of this particular spacer the row again ends with an introversion such that either again such a spacer can be fitted or a seed can be fitted.

5 The invention also relates to a connector for forming a row as disclosed hereinbefore.

A particular embodiment of a connector according to the invention is characterised in that cross-sectional dimensions of an introversion are fractionally smaller than cross-sectional dimensions of a seed, in that the connector is manufactured of somewhat flexible material and in that at least over part of the length of an introversion and going from the end at which the introversion is present a slit has been provided which in a direction perpendicular to a longitudinal direction of the connector stretches from the outside
10 of the connector to the introversion.
15

Thereby it is achieved that a mechanical clamping takes place of a radioactive seed and a non-radioactive spacer, respectively, which have been put in the relevant introversion.

The invention will now further be described with reference
20 to the accompanying drawings in which:

Figure 1 shows, on an enlarged scale, a seed/spacer;

Figure 2 shows a connector with introversions at both ends;

Figure 3 shows a connector having an introversion at one end and having at an other end a shape identical to the shape of a
25 seed;

Figure 4 shows a row of radioactive seeds and non-radioactive spacers with a predetermined pitch in a hollow needle with an open end, closed with a plug of wax;

Figure 5 shows a row of radioactive seeds and non-radioactive spacers arranged with a certain pitch according to another
30

embodiment in a hollow needle an open end of which is closed with a plug of wax;

Figure 6 shows schematically how a row of radioactive seeds and non-radioactive spacers can be put together with connectors according to figure 2;

Figure 7 shows how a row of radioactive seeds and non-radioactive spacers can be put together by means of connectors according to figure 2 and 3.

Referring to figure 1 reference number 1 indicates the general shape of seeds. The seed has an elongated shape in which dimension L in longitudinal direction is of the order of 4,5 mm and in which the diameter D is of the order of 1 mm or smaller. In one embodiment of the invention the spacers are of the same dimensions as the seeds shown in figure 1. In another embodiment of the invention the spacers are shaped as shown in figure 3 to be discussed later on. In order to arrange seeds and spacers of the shapes and dimensions as shown in figure 1 into a row, such as described in the introduction, with a predetermined pitch, which row is physically coherent, connectors can be used such as shown in figure 2 with reference number 2. Connector 2 has been manufactured of bio-absorbable material, which in this field is an known group of materials. Element 2 has an elongated shape and is provided at both ends 3 and 4, respectively with introversions 5 and 6, respectively. Also element 2 of the embodiment shown in figure 2 has been provided all along its length with a slit 7. Element 2 is also provided with a connecting opening 8 between the introversions 5 and 6 and the slit 7 extends from the outside of the connector 2 to the introversions 5 and 6 and the connecting space 8 between said introversions. It is noted that the existence of the connecting space is optional as well as the slit 7 being continuous. Other embodiments of a connector 2 with

introversions 5 and 6 at both ends 3 and 4 are made up by connecting space 8 not being present and/or by slit 7 not being continuous from end 3 to end 4. In the latter case the connector 2 comprises two slits at the location of the slit parts 7A and 7B of slit 7, which two slits are not connected together. The two slits mentioned in each case run from the outside of connector 2 to the introversions 5 and 6, respectively. Another embodiment of a connector 2 such as shown in figure 2 is made up by a connector in which no slit 7 is present at all.

In case connector 2 is provided with a continuous slit 7 or with two non-continuous slits at the location of the slit parts 7A and 7B the introversions 5 and 6 are somewhat flexible as a result of the presence of the slit and slits, respectively. In that case the diameter of the introversions 5 and 6 is fractionally smaller than the diameter D of a seed or a spacer. As a consequence, there is advantageously a slight degree of clamping which is favourable for the physical coherence of the row of radioactive seeds and non-radioactive spacers arranged with connectors 2. In the case of neither a continuous slit 7 nor two separate slits at the location of the slit parts 7A and 7B the shapes of the introversions 5 and 6 are not flexible. In that case the inner diameters of the introversions 5 and 6 should be fractionally larger than the diameter D of the radioactive seeds and non-radioactive spacers respectively, such as shown in figure 1 and/or in figure 3.

The choice to apply a slit 7 or two slits at the locations of the slit parts 7A and 7B is amongst others dependant upon the flexibility of the bio-absorbable material from which connector 2 has been manufactured. The stiffer the relevant material, the more need for slits 7.

The total length of connector 2 is indicated by Z. The lengths of introversions 5 and 6 are smaller than the length of a seed 1, preferably, but not necessarily, smaller than half the length of a seed 1. Preferably, but not necessarily, the lengths of the introversions 5 and 6 are equal. That has as an advantage that in composing an arranged row of radioactive seeds and non-radioactive spacers the orientation of the connector 2 in a row does not play a role. Logistically that produces advantages since in the processing of the connectors 2, such as in filling apparatus appropriate for composing an arranged row of radioactive seeds and non-radioactive spacers the orientation of the connector 2 does not have to be looked at.

In figure 1 a first embodiment of a spacer has been shown, namely that one having outer dimensions identical to the outer dimensions of a seed. Figure 3 shows a second embodiment of a spacer. Spacer 10 shown in figure 3 comprises a part 11 having a length Z equal to the length Z of a connector 2 shown in figure 2. Further connector 10 comprises a projection 12 at the first end 13 and an introversion 14 at the second end 15 of the part 11. Projection 12 has the outer shape and dimensions of a part of a seed such as shown with reference number 1 in figure 1. The diameter of projection 12 is equal to the diameter D of a seed 1 and the length of projection 12 is smaller than or equal to half the length L of a seed 1. The length of introversion 14 is at most half the length L of a seed 1. The inner diameter of introversion 14 is substantially equal to the diameter D of the seed 1. Similarly to connector 2 connector 10 can be provided with a longitudinal slit 16 running from the outside of connector 10 to the inside of the introversion 14 and stretching along the length from the end 15 until at least part of the introversion 14. Slit 16 however can run amply into the projection 12 such as shown in the

exemplary embodiment of connector 10 in figure 3. Similarly to connector 2 connector 10 is manufactured of bio-absorbable material; and amongst others the flexibility of the bio-absorbable material plays a role in the choice of applying a slit 16 of a certain length.

5 In case a slit 16 is applied, the inner diameter of the introversion 14 is fractionally smaller than the diameter D of a seed 1 and a projection 12, respectively and in case no slit 16 is applied the inner diameter of the introversion 14 is fractionally larger than the diameter D of a seed 1 and a projection 12, respectively.

10 Figure 4 shows the way in which the physically coherent row of radioactive seeds and non-radioactive spacers arranged with the predetermined pitch can be put together by means of connectors 2 such as shown in figure 2. For distinction purposes seeds have been indicated in figure 4 as longitudinal shapes with a dashed rectangle
15 inside while spacers have been indicated as longitudinal shapes only such as shown in figure 1. Reference number 20 schematically shows a hollow needle provided with an open end 21, which end has been shut with a plug of wax 22 in an known way. An arranged row of radioactive seeds 24, 25, 26, 27, and 28 with non-radioactive spacers 29, 30, 31,
20 32 and 33 between them has been shown in the hollow needle 20. The radioactive seeds and non-radioactive spacers are separated by connectors 34, 35, 36, 37, 38, 39, 40, 41 and 42. The connectors 34-42 are connected such as described in more detail in connection with figure 2. The connectors 34-42 take care of the desired physical
25 coherence between the radioactive seeds and non-radioactive spacers of the arranged row 23. As a consequence of the identity of the longitudinal dimensions of the radioactive seeds and the non-radioactive spacers at a length Z of the connector 34-42 the arranged row 23 has a pitch S which is the same over the whole length of the
30 arranged row 23. In connection with the pressing of the row 23 against

the plunger, schematically shown with reference number 43, at the retraction of the needle 20 in the direction of the arrow 44 the end of the row 23 in touch with the plunger 43 can be made up of an extra connector 45.

5 Figure 5 again shows the same arranged row of radioactive seeds and non-radioactive spacers shown in figure 4 in which, however, in place of spacers according to the model shown in figure 1 use has been made of spacers according to the model shown in figure 3. Same elements as in figure 4 have been indicated with the same reference
10 number. However, the combinations of spacers 29 with connector 36, spacer 30 with connector 38, spacer 31 with connector 39, spacer 32 with connector 40 and spacer 33 with connector 42 have been replaced by spacers 46 and 47 and 48 and 49 and 50, respectively. The number of
15 elements to be pushed together in a row 23 according to figure 5, using spacers according to figure 3, is considerably smaller than the number of elements to be pushed together in making up an arranged row as shown in figure 4 with separate seeds, separate spacers and separate connectors.

 Figures 6 and 7 show schematically in which way, starting
20 from a store with radioactive seeds, a store with connectors and a store with spacers an arranged row of radioactive seeds and non-radioactive spacers can be put together. In figure 6 one starts with radioactive seeds and non-radioactive spacers according to the model shown in figure 1 and connector shown in figure 2. In figure 7 one
25 starts with radioactive seeds according to the model shown in figure 1, spacers according to the model shown in figure 3 and connectors according to the model of shown in figure 2.

 Figure 6 shows three stores, a store 51 with schematically shown therein a number of seeds 52 and 53, a store 54 with shown
30 schematically therein a number of spacers 55 and 56 and a store 57

with shown schematically therein an number of connectors 58 and 59, according to the model shown in figure 2. The stores 51, 54 and 57 have been provided with means to transport the radioactive seeds, non-radioactive spacers and connectors, respectively therein in the direction of a position in which an arranged row of the relevant seeds and spacers can be made up. For example, a device can be used such as disclosed in more detail in Dutch patent application 1012697 and United States patent application 09/377,382, respectively the contents of which applications are incorporated herein by reference. Each time a radioactive seed or a non-radioactive spacer has to be added to an already existing row of radioactive seeds and non-radioactive spacers, respectively each time a radioactive seeds is to form the first element of such row a radioactive seed and a non-radioactive spacer, respectively are transported from store 51 and store 54, respectively to a location where a putting together can take place of the relevant radioactive seed and the non-radioactive spacer, respectively with a connector according to the model disclosed in connection with figure 2 from the store 57. Reference number 60 indicates that by means of a plunger 62 a connector 63 and a radioactive seed 64 are linked up to a whole 65. The radioactive seed 64 either is the first element in an arranged row of radioactive seeds and non-radioactive spacers or is added to an already existing arranged row. In the latter case the radioactive seed 64 is pushed by the plunger 62 into an introversion of a previous connector at the end of the row mentioned, schematically indicated with the reference number 66.

Reference numeral 61 refers to the same course of things sketched in relation to the adding of a spacer 67 to an already existing row, the last connector of which has been indicated by reference numeral 66. Similarly to the description hereinbefore relating to a radioactive seed 64 the movement of a plunger 62 links

up a connector 63 to a non-radioactive spacer 67 to a unit 68 which is brought into connection with the element 66 by the plunger 62.

In figure 7 elements already designated in figure 6 have been shown with the same reference numerals as used in figure 6. Store 54 with spacers 55 and 56 of the same shape and dimensions as the radioactive seeds is not present in figure 7 while a store 69 is present with a supply of spacers 70 and 71 according to the model of figure 3. Reference number 60 similarly to figure 6 shows linking up of a connector 63 according to the model shown in figure 2 with a radioactive seed 64 to a unit 65 which may form the forward end of an arranged row or may be added to an already existing arranged row the last element of which is shown in dashed lines with reference numeral 66. Reference number 75 shows how a combination of a radioactive seed 66, a connector 63 according to the model shown in figure 2 and a spacer 72 according to the model shown in figure 3 can be linked up in one stroke and can form the beginning of a newly to be formed row or can be added to an already existing row the last element of which is a connector according to figure 2 or a spacer according to figure 3 and in which the radioactive element can be pushed into the introversion 77 thereof. On putting together a unit 74 comprising a radioactive seed 64, a connector 63 according to the model shown in figure 2 and a spacer 72 according to the model shown in figure 3 an element is transported from each of the stores 51, 57 and 69 to a trajectory of the plunger 62. Subsequently the plunger 62 is operated to press the elements 64, 63 and 72 together to an element 74.

Reference numeral 76 indicates which actions are taken when two or more subsequent spacers of the model shown in figure 3 have to form part of an arranged row of radioactive seeds and non-radioactive spacers. In that case for each spacer to be added to an already existing row a spacer 72 is transported in the trajectory of the

plunger 62, which spacer 72 subsequently forms an element 73 that is being coupled to an already existing end 72' of a previous spacer of the same model.

5 After the foregoing many possibilities for executing the invention will be obvious for the person skilled in the art. All these embodiments are considered to embody the invention which has been put under protection according to the accompanying claims.

CLAIMS

1. Row of radioactive seeds and non-radioactive spacers arranged with a predetermined pitch, in which the number of spacers
5 can be equal to zero, for a brachytherapeutic treatment of an animal body with radioactive radiation, which seeds have elongated shapes, characterised in that connectors are present between subsequent seeds, which connectors have substantially elongated shapes with two ends, in that at least one end of each connector is provided with an
10 introversion in a longitudinal direction of the connector, in that the introversion has a shape complementary to the shape of the seed and in the longitudinal direction of the connector has a dimension which is less than the length of a seed.

2. Row according to claim 1 characterised in that seeds and
15 spacers have identical shapes and dimensions and that each end of each connector is provided with an introversion in longitudinal direction of the connector and in that each introversion has a shape that is complementary to the shape of a seed and in the longitudinal direction of the connector has a dimension smaller than the length of a seed.

3. Row according to claim 1 characterised in that one or more
20 spacers comprise connectors, one end of which is provided with the introversion and an other end of which is provided with a projection having a shape identical to the shape as from an end of a seed.

4. Row according to claim 3 characterised in that the length
25 of the projection is smaller than half the length of a seed.

5. Row according to one of the preceding claims, characterised in that a dimension of the introversion in the longitudinal direction of the connector is at most equal to half of the length of a seed.

6. Connector for putting together a row as described in one of
30 the previous claims.

7. Connector according to claim 6 characterised in that cross-sectional dimensions of the introversion are fractionally smaller than cross-sectional dimensions of the seeds, in that the connector is manufactured of somewhat flexible material and that at least along a part of the length of an introversion and running from the end at which the introversion is present a slit is provided, which extends in a direction perpendicular to the longitudinal direction of the connector from the outside of the connector to the introversion.

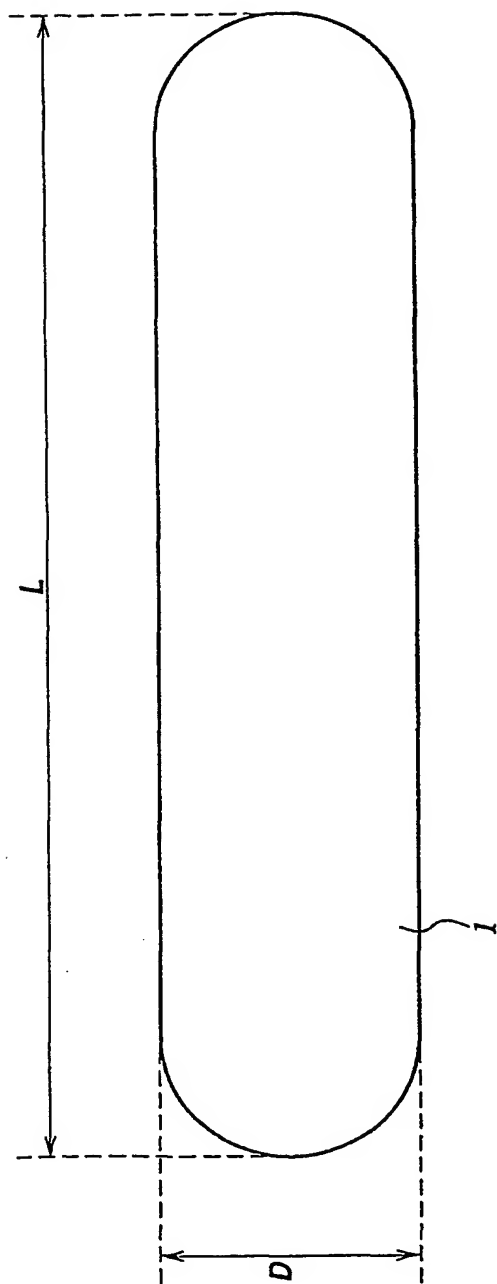


Fig. 1

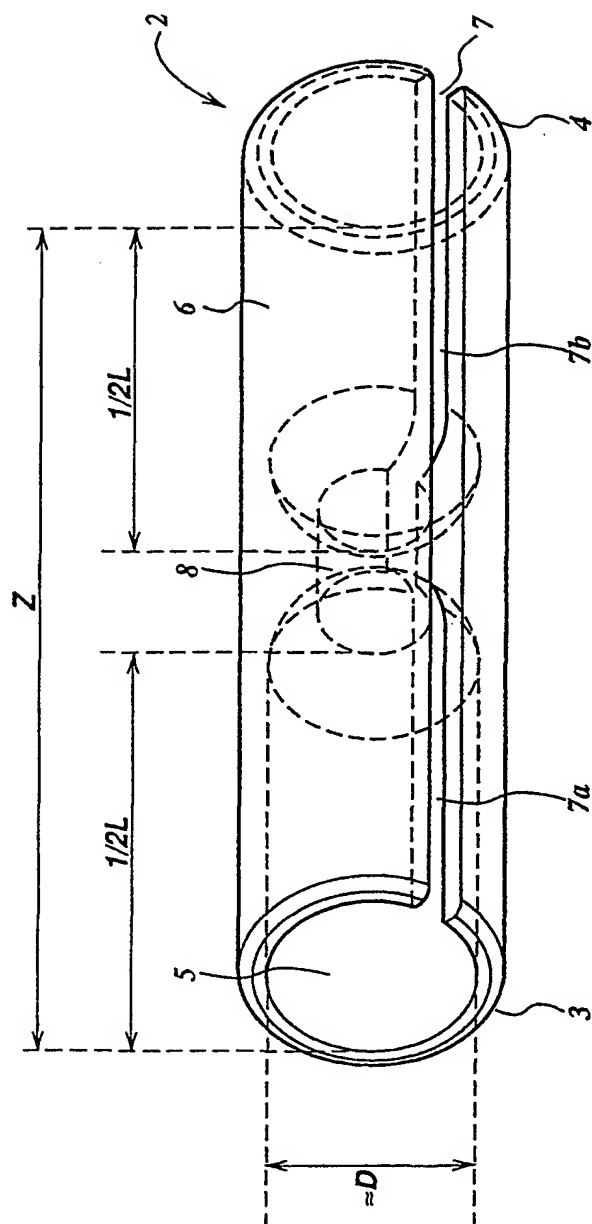


Fig. 2

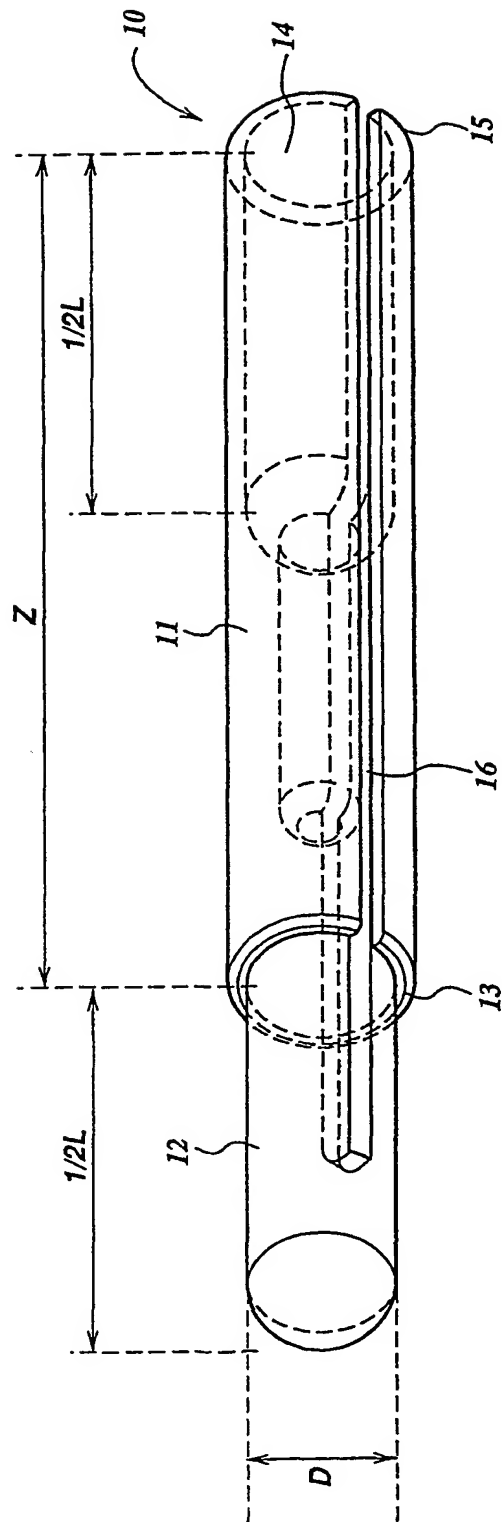


Fig. 3

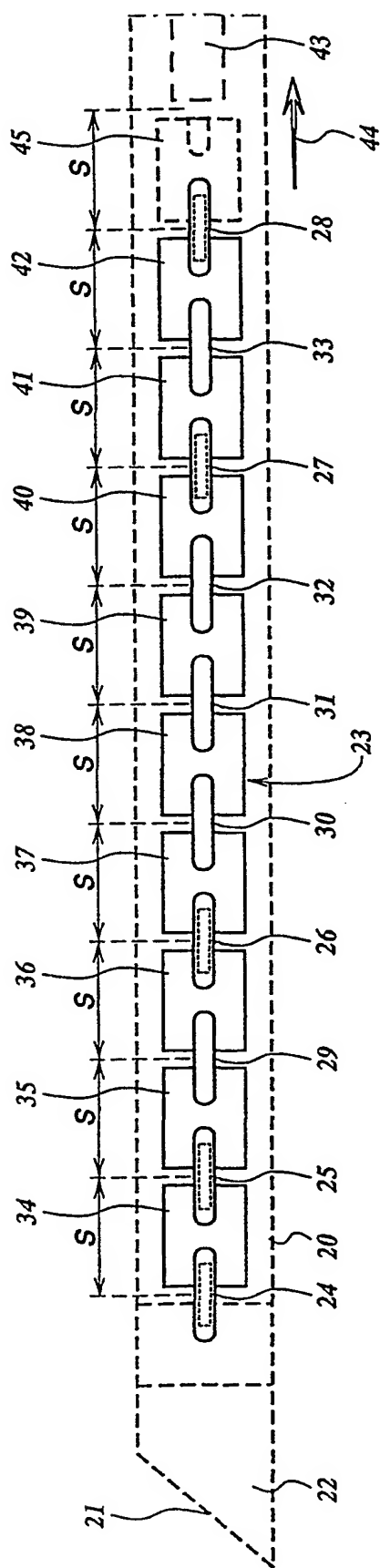


Fig. 4

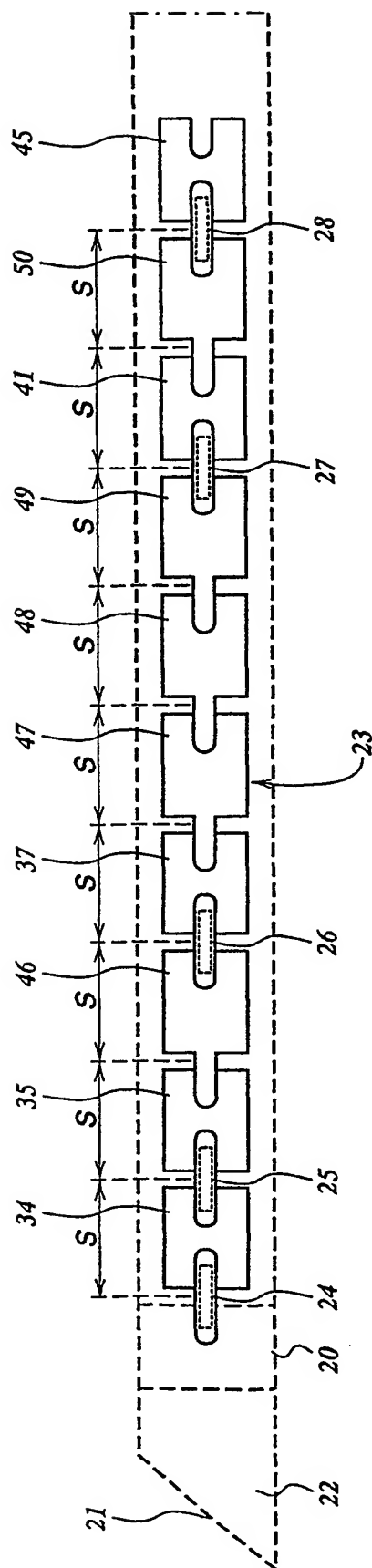


Fig. 5

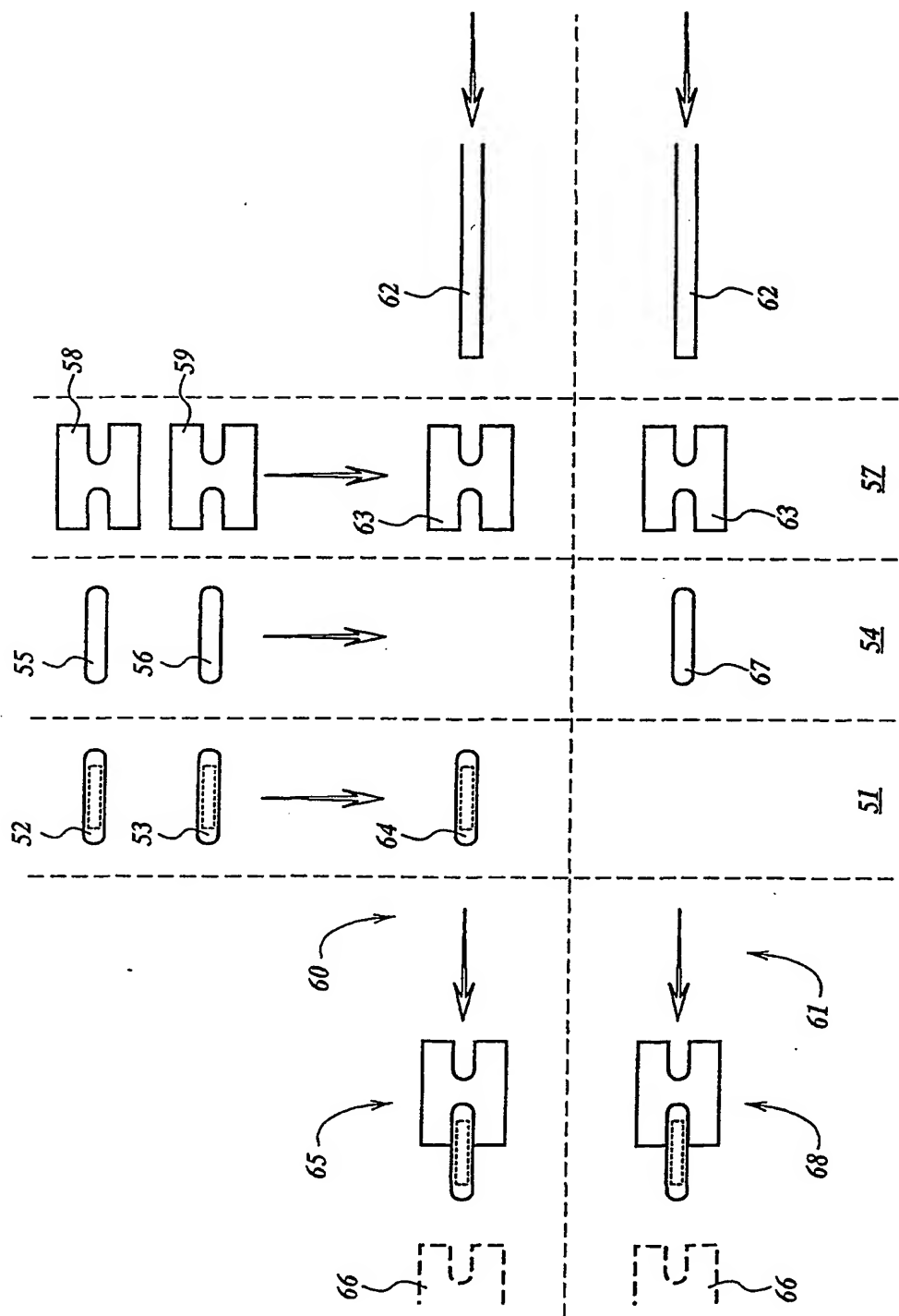


Fig. 6

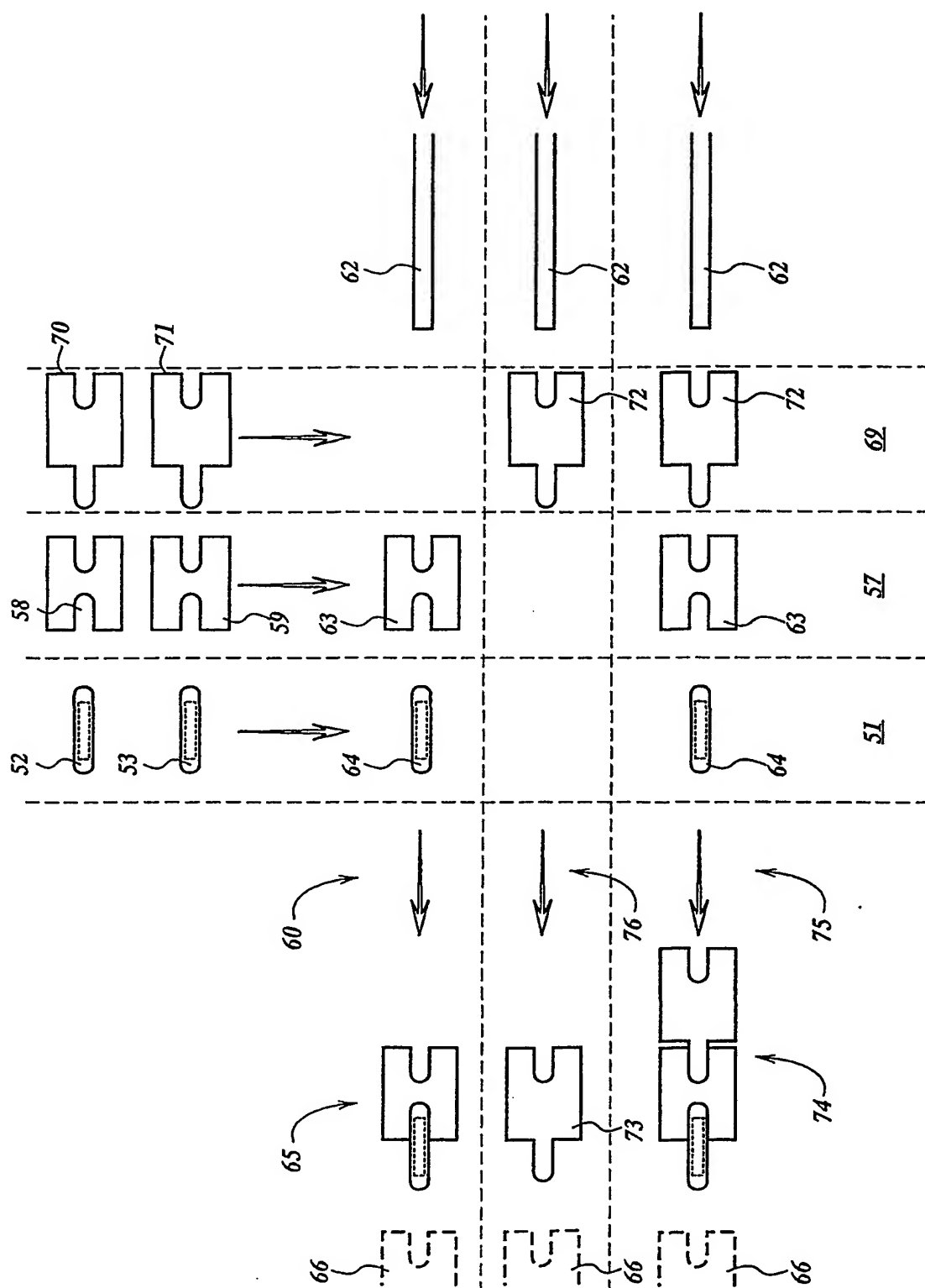


Fig. 7

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 01/00647

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61N5/10 A61M36/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61N A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 59675 A (GRIMM PETER D) 25 November 1999 (1999-11-25) cited in the application page 3, line 16 -page 6, line 10; figures 1,2	1,2,5,6
Y A	---	3,4 7
Y	US 4 815 449 A (HOROWITZ BRUCE S) 28 March 1989 (1989-03-28) cited in the application column 4, line 30 - line 40	3,4
X	WO 00 09211 A (JAHRMARKT SCOTT L ;SMITH SCOTT T (US); SYNTHEON LLC (US); SLATER C) 24 February 2000 (2000-02-24) cited in the application page 10, paragraph 3; figure 12 --- -/--	1,2,5,6

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

28 November 2001

Date of mailing of the international search report

05/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Petter, E

INTERNATIONAL SEARCH REPORT

In
tional Application No
PCT/NL 01/00647

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 6 273 851 B1 (JAHRMARKT SCOTT L ET AL) 14 August 2001 (2001-08-14) figures 2-9	1,2,5,6
P,X	US 6 264 599 B1 (JAHRMARKT SCOTT L ET AL) 24 July 2001 (2001-07-24) column 7, line 6 - line 34; figures 11-13	1,2,5,6

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/NL 01/00647

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9959675	A	25-11-1999	US	6010446 A	04-01-2000
			WO	9959675 A1	25-11-1999
US 4815449	A	28-03-1989	US	4697575 A	06-10-1987
			AT	119404 T	15-03-1995
			DE	3751143 D1	13-04-1995
			EP	0292630 A1	30-11-1988
WO 0009211	A	24-02-2000	US	6080099 A	27-06-2000
			AU	1196400 A	06-03-2000
			WO	0009211 A1	24-02-2000
			US	6273851 B1	14-08-2001
US 6273851	B1	14-08-2001	US	6080099 A	27-06-2000
			AU	1196400 A	06-03-2000
			WO	0009211 A1	24-02-2000
US 6264599	B1	24-07-2001	NONE		